A RETROSPECTIVE COHORT STUDY OF DIABETES MELLITUS AND ANTIPSYCHOTIC TREATMENT IN THE UNITED KINGDOM
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OBJECTIVE: In this retrospective cohort study, we explored the UK General Practice Research database (GPRD) to determine the hazard ratio of diabetes mellitus (DM) for patients prescribed antipsychotics compared with the GPRD general patient population in the UK.

METHODS: An antipsychotic cohort comprised of patients exposed to both conventional and atypical antipsychotics (N = 46,111), individual antipsychotic cohorts comprised of patients exposed to a single antipsychotic, and a general patient population cohort (N = 266,272) derived from the GPRD database were studied. A Cox proportional hazards regression model was used to determine the hazard ratio (HR) of diabetes development between these cohorts. The covariates included in the model were age, gender, and the presence or absence of obesity.

RESULTS: Compared to the GPRD general patient population cohort, patients exposed to antipsychotics had a higher risk of developing diabetes (HR = 1.5; CI = 1.1–1.9). The risk of developing diabetes during exposure to thioridazine and risperidone was significantly higher than that of the GPRD general patient population. Assessment of other antipsychotics was limited by sample size of the cohorts.

CONCLUSIONS: Patients exposed to antipsychotic drugs have an increased risk of developing diabetes. It remains unclear to what extent the increased risk of diabetes is related to treatment factors or factors related to the underlying psychiatric conditions commonly treated with antipsychotic drugs.

IMPROVEMENTS IN LIFE EXPECTANCY WITH LIFESTYLE CHANGES OR METFORMIN IN OVERWEIGHT, GLUCOSE INTOLERANT PATIENTS: A MODELING STUDY OF THE LONG-TERM IMPLICATIONS OF THE DIABETES PREVENTION PROGRAM
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OBJECTIVES: The Diabetes Prevention Program (DPP) investigated the effects of intensive lifestyle changes (LsC) or metformin (MET) on delaying the onset of type 2 diabetes in overweight patients with impaired glucose tolerance (IGT). Patients randomized to either LsC or MET 850 mg twice daily reduced their risk of developing type 2 diabetes by 58% and 31% respectively, compared to controls. A simulation model was developed to explore the long-term implications of delaying onset of type 2 diabetes with LsC or MET.

METHODS: A Markov model combined data from DPP with published data on mortality of IGT patients compared to type 2 diabetes, in order to calculate the possible long-term effects of delaying the onset of diabetes with LsC or MET on life expectancy (LE). The model simulated 3 states. “IGT”, “type 2 diabetes”, and “dead”. Annual transition probabilities for each treatment arm were derived from the DPP, population studies, and national mortality statistics. LE was calculated for each treatment arm. Different assumptions were tested regarding the post-trial effect of the delay of onset of diabetes. Additional sensitivity analysis was performed to identify other parameters with important impacts on LE.

RESULTS: Using the conservative assumption, LE from baseline age of 51 years was 22.95, 23.12, and 23.03 years for the control, LsC, and MET groups respectively. Using the optimistic assumption, LE further improved by 0.39 and 0.14 years for the LsC and MET groups respectively. Other parameters with important impacts on LE were the mortality rates in the states of “IGT” and “type 2 diabetes”.

CONCLUSIONS: Interventions that delay the onset of type 2 diabetes in overweight IGT patients may lead to important improvements in LE.

OUTCOMES WITH ROSIGLITAZONE IN CLINICAL PRACTICE
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OBJECTIVES: Unlike older agents, rosiglitazone lowers blood glucose levels by directly acting on insulin resistance, the primary metabolic defect of type 2 diabetes, and has other positive metabolic effects on lipids and blood pressure. Outcomes of patients on rosiglitazone used as combination and monotherapy in routine Canadian clinical practice is reported.

METHODS: Five Canadian centers participated in retrospective data collection. Charts were reviewed for over 635 patients on rosiglitazone with the use of a software program designed to track outcomes pre and post Avandia treatment such as glycemic control, metabolic parameters (including renal function, liver enzymes, and lipids) as well as weight, blood pressure and changes in diabetic medications. Patient data were entered into the software and analyzed using standard statistical methodology.

RESULTS: In the analysis of 337 patients on rosiglitazone, the average age was 71.6 years with 44% females. Rosiglitazone was started as additional therapy to sulphonylureas (38%) or metformin (42%) or both (33.5%). There were 150 patients on rosiglitazone as monotherapy (44%). The relative reduction in HbA1c was 15.3% at
best and 12% at end. Changes in renal function and liver enzymes were not statistically significant. There was a significant improvement in LDL and blood pressure while on rosiglitazone. There were eight patients with elevations of liver enzymes.

CONCLUSIONS: In routine Canadian clinical practice, rosiglitazone is effective at lowering both FBG and HbA1c significantly over time and appear to be comparable to, or better than, those reported for the established oral agents. Many patients were able to reach improved targets of HbA1c and FBG with no reported serious adverse events. Further study is required to investigate the beneficial metabolic effects observed on blood pressure and lipids.

**Diabetes—Economic Outcomes Presentations**

**The Economic Value of Non-Dihydropyridine vs. Dihydropyridine Calcium Channel Blocker/Ace Inhibitor Combinations in Patients with Type-II Diabetes**

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OBJECTIVE: Combination therapy with angiotensin-converting enzyme inhibitors (ACE-I)/calcium channel blocker (CCB) has been recommended for hypertensive diabetics. This study assessed the cost-effectiveness of an ACE-I/non-dihydropyridine CCB (ACE-I/NDCCB: Trandolapril/Verapamil or T/V) relative to an ACE-I/dihydropyridine CCB (ACE-I/DCCB: Benazepril/Amlodipine or B/A) for the treatment of patients with diabetics, who frequently also have hypertension.

METHODS: We have adapted a previously published Markov model that simulated the disease progression of a hypothetical cohort newly-diagnosed diabetes patients towards end-stage renal disease (ESRD). The model was developed from a payer perspective and estimated the discounted drug and ESRD costs and quality adjusted life years (QALYs) over a 3-year, 5-year and lifetime time horizon. The baseline analysis conservatively assumed that all patients, regardless of treatment received, progressed from normoalbuminuria to microalbuminuria (progression rate = 0.011), to gross proteinuria (progression rate = 0.026), and to ESRD (progression rate = 0.034). Given clinical evidence demonstrating greater reductions in baseline proteinuria with T/V than with B/A (urinary albumin excretion ~65% versus ~25%, respectively), the least conservative scenario assumed that patients receiving T/V would progress less rapidly than patients receiving B/A.

RESULTS: In the baseline analysis, T/V resulted in lower net costs than B/A. The cost advantage per hypertensive diabetic is $92, $141 and $743 in favor of T/V over a three-year, five-year and lifetime time frame respectively. When the most extreme clinical difference is assumed, T/V treatment results in $168, $313 and $2,293 in net savings per diabetic over the respective time periods while also providing a small net benefit in QALYs (.000632, .0018, .063 QALYs per patient).

CONCLUSIONS: From a payer perspective, T/V is cost-saving relative to B/A for the management of hypertensives with diabetes under both scenarios. These savings are driven by the lower cost of drug and the reduced resources required for ESRD treatment.

**Prevention of Type 2 Diabetes in the USA: Cost-Effectiveness Issues**

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OBJECTIVES: Onset of Type 2 diabetes (T2D) can be delayed by lifestyle changes and/or medications. Forecasts predict an epidemic of new cases of T2D as the population ages, and modern lifestyles become increasingly unhealthy. T2D patients have >double mortality rates and higher treatment costs of matched non-diabetics. A model was developed to assess acceptable cost limits for a general population-targeted program aimed at reducing the incidence of T2D by 10%.

METHODS: A Markov model simulated the incidence of and increased direct medical costs and mortality associated with T2D. Data were derived from published sources. Costs and life expectancy (LE) calculated (discounted at 3% p.a.). Analyses assessed the maximum costs/person a payer could outlay to achieve a 10% reduction in T2D incidence a) without increasing the healthcare budget, and b) remaining within an attractive incremental cost-effectiveness (ICER) <$50,000/life year gained. A health insurance perspective was taken. Sensitivity analysis identified parameters with important impacts on outcomes.

RESULTS: A diabetes prevention intervention aimed at a general population with mean age 50 years that reduces incidence of T2D by 10% would improve LE by 0.05 years per person. Up to a cost of $55/year/person, the program would result in overall cost savings due avoidance of higher costs associated with T2D. The ICER of the program would be <$50,000 at a cost of $2.50/person/year. Sensitivity analysis revealed that age of target population, effectiveness of intervention, incidence of diabetes, and increase in mortality with diabetes have a large influence on the results.

CONCLUSIONS: Diabetes prevention programs aimed at a general population could be cost saving or cost-effective if the costs of the program do not exceed limits identified. In other, higher-risk populations, such as glucose intolerant or racial sub-groups, where the incidence of diabetes and effects of intervention are greater, these cost limits are could be higher.